that differences between rRNA molecules tend to be clustered within specific regions. Probes targeting disclosed regions of variability are especially important since they may be used to differentiate between even closely related organisms. *See, e.g.*, specification at pages 10-12. Applicants' discovery of these variable regions as potential target sites for distinguishing between organisms is generously supported in the specification by over sixty specific probe sequences and approximately twenty different target groups ranging from individual species to whole genuses to phylogenetically diverse bacteria and fungi. *See* Examples section at pages 25-118.

To find these regions of predicted variability for a given target organism or group of organisms, a partial or complete ribosomal subunit sequence for each target organism, as well as for phylogenetically near neighbors or expected non-target organisms, must first be obtained from a sequence database or published literature or, alternatively, some or all of the sequences may be determined using sequencing procedures well known in the art. *See, e.g.*, specification at paragraph bridging pages 10 and 11. These sequences then need to be aligned with each other and with the corresponding ribosomal subunit sequence of *Escherichia coli* or *Saccharomyces cerevisiae* identified in Figures 1-5 so that homology between them is maximized. Alignment and comparison with all or a portion of the corresponding ribosomal subunit sequence of *Escherichia coli* or *Saccharomyces cerevisiae* is performed in order to locate the target regions which were found by Applicants to more likely contain variable regions. *See, e.g.*, specification at paragraph bridging pages 12 and 13. Probes targeting variable regions should be designed to maximize homology to the target sequence or sequences and minimize homology to the non-target sequence or sequences. Specific probe design criteria and construction are fully detailed in the specification at pages 12-22.

All of the claims of the instant application are directed to methods for determining whether a variable region characteristic of nucleic acid of one or more non-viral target species is present in a sample. The claims clearly indicate that this distinguishing variable region is contained within one of a number of specifically defined target regions corresponding to regions of *E. coli* 5S,

16S or 23S rRNA (or the encoding DNA). The presence of a variable region characteristic of nucleic acid of one or more target species in a sample can be detected with hybridization assay means or an oligonucleotide probe which provides an indication that at least one member of the target species is present in the sample. The hybridization assay means and oligonucleotide probes of the claimed methods can distinguish nucleic acid of the target species containing the variable region from nucleic acid of one or more non-target species which may be present in the sample.

Applicants submit that the cases relied upon by the Examiner in support of the written description rejection are nonanalogous to the particulars of the subject application. For instance, one of the primary cases relied upon by the Examiner is *University of California v. Eli Lilly and* Co., 43 USPQ2d 1398 (Fed. Cir. 1997), which concerns *inter alia* claims directed to a microorganism containing a human insulin cDNA. While conceding that the patent disclosed a general method for obtaining the human cDNA, along with the amino acid sequences of human insulin A and B chains, the court in *Lilly* found no distinguishing information concerning the identity of the claimed cDNA. *Id.* at 1405. In other words, the court found that the patentee had identified the claimed cDNA by name and function alone without supplying any distinguishing structural details regarding the cDNA. Because the patent disclosure in *Lilly* was completely devoid of *any* relevant structural or physical characteristics of the claimed cDNA, the court concluded that the patentee had failed to provide sufficient identifying information to satisfy the written description requirement.

Unlike *Lilly*, or any of the other cases identified in the Examiner's Office Action, the claims of the present invention are directed to methods of use rather than compositions *per se*. The claimed methods include contacting a sample with hybridization assay means or an oligonucleotide probe which can detect a variable region characteristic of one or more non-viral target species. The claims indicate that this variable region is located in a specifically defined target region identified by the corresponding region in an rRNA sequence of *E. coli*, or the encoding DNA, as set forth in Figures 1-3. These target regions were among those discovered by Applicants to have the greatest

variability between the ribosomal nucleic acid sequences of differing organisms as distinguished from all other potential target regions. Armed with this distinguishing information regarding the identity of the target regions, those having ordinary skill in the art will be able to readily identify the precise sequences of these target regions for any given target or non-target species having known ribosomal nucleic acid sequences. And, as specified in the claims, the variable regions being targeted by the claimed hybridization assay means or oligonucleotide probes are contained within these target regions. Thus, given the nature of the claimed invention, the claims type (*i.e.*, method of use claims), and the distinguishing structural details set forth in the claims and specification, Applicants submit that additional sequence information should not be required to evidence that they were in possession of the invention claimed at the time the application was filed.

For the reasons detailed above, Applicants submit that the claims of the subject application are fully supported by an adequate written description under 35 U.S.C. § 112, first paragraph. Accordingly, withdrawal of the Examiner's rejection is respectfully requested.

The title of the invention has been amended herein to be more consistent with the language of the presently pending claims.

Claims 486-491 have been amended herein solely to make editorial changes. The scope of the claims has not been further limited by these amendments and no amendment has been made for a reason related to patentability.

Conclusion

Applicants submit that the subject application is in condition for allowance and Notice to that effect is respectfully requested.

Accompanying this Response is a Petition for Extension of Time (one month). Please charge the extension of time fee and any other fees which may be due in connection with this Response to Deposit Account 07-0835.

Certificate of Mailing

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is being deposited on the date indicated below with the U.S. Postal Service as First Class Mail addressed to the Commissioner for Patents, Washington, D.C. 20231.

Respectfully submitted,

Date: February 2, 2001

By: _____

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